

a 3 3.) Page 7, please replace paragraph 1 (lines 1-2) with:

-- Figure 10 shows the generation of esDC stably transfected with GFP following introduction of the transgene into the parent ES cell line.

Detailed Description of the Invention --

a 4 4.) Page 25, please replace paragraph 1 (line 1) with:

-- Claims

We claim: --

a 5 5.) Please insert the annexed new page 29, containing the following:

-- Abstract of the Invention

Disclosed are embryonic stem cell-derived dendritic cells, genetically modified immature dendritic cells capable of maturation, as well as methods for the production of such cells. In one embodiment, the cells made be produced by a method comprising the steps of providing a population of embryonic stem cells; culturing the embryonic stem cells in the presence of a cytokine or combination of cytokines which brings about differentiation of the embryonic stem cells into dendritic cells; and recovering the dendritic cells from the culture. In a further embodiment, the cells may be genetically modified. --

B. In the claims:

a 6 1.) Canceled claims

Please cancel claims 1-63, without prejudice.

2.) New claims

Please add new claims 64-104 as indicated below.

Clean Version of Pending Claims

64. A process for producing a long-term culture of immature dendritic cells, which process comprises:
- (i) providing a population of embryonic stem cells;
 - (ii) culturing the embryonic stem cells in the presence of a cytokine or combination of cytokines which bring about differentiation of the embryonic stem cells into immature dendritic cells to produce a long-term culture of immature dendritic cells; and
 - (iii) recovering immature dendritic cells from the culture, which immature dendritic cells are capable of maturation to an immunostimulatory phenotype.
- Sub C1)
- Q6
65. The process of claim 64 further comprising the step (iv) of stimulating the immature dendritic cells to mature thereby producing mature immunostimulatory dendritic cells.
66. The process of claim 65 wherein the immature dendritic cells are stimulated to mature with an inflammatory mediator.
67. The process of claim 65 wherein the inflammatory mediator is LPS.
68. The process according to claim 64, wherein the cytokine or combination of cytokines is or includes IL-3.
69. The process according to claim 68, wherein a combination of cytokines including IL-3 and GM-CSF is used.
- Sub C2)
70. The process according to claim 64, wherein the embryonic stem cells in (i) are in the form of embryoid bodies.
71. The process according to claim 64, wherein the embryonic stem cells are genetically modified.

72. The process of claim 71, wherein the cells express one or more heterologous gene(s).
73. The process of claim 72, wherein the one or more heterologous gene(s) encode a protein which has an immunomodulatory effect.
74. The process of claim 73, wherein the protein is a cell surface receptor.
75. The process of claim 74, wherein the protein is Fas-ligand.
76. The process of claim 72, wherein the one or more heterologous gene(s) express a dominant negative form of an endogenous protein.
77. The process of claim 73, wherein the protein is an antigen target for the immune system, such as an autoantigen, a tumour antigen, or a foreign antigen.
78. The process of claim 64, wherein the cell co-expresses two or more heterologous genes.
79. The process of claim 78, wherein one of the heterologous genes prolongs the life-span of the cell.
80. The process of claim 79, wherein the gene is an anti-apoptotic gene.

sub 8' 81. ~~The process of claim 78 or 79 wherein the gene encodes FLIP or bel-2.~~

82. The process of claim 64, in which one or more endogenous gene(s) have been inactivated.

83. The process of claim 82, wherein the inactivated endogenous gene(s) comprise any of: B7-1, IL-12, and the p35 or p40 subunit of IL-12.

84. The process of claim 71, wherein the embryonic stem cells are transfected with at least one gene which is expressed in the dendritic cells.

85. The process of claim 84, wherein the gene is under the control of a promoter which initiates or upregulates gene expression on maturation of dendritic cells.

Sub B 86. The process of claim 84 or claim 85, wherein the gene is a reporter gene which expresses a detectable product in the dendritic cells.

Q 6 87. The process of claim 86, wherein the gene encodes a fluorescent product.

88. The process of claim 87, wherein the gene is the GFP gene.

89. The process of claim 71, wherein the ES cells are genetically modified so as to inactivate at least one copy of at least one gene.

90. The process of claim 64, wherein the recovered immature dendritic cells are substantially pure.

91. The process of claim 64, wherein the cells are lymphoid.

92. The process of claim 64, wherein the cells are myeloid.

93. The process of claim 64, wherein the cells are human.

94. The process of claim 64, wherein the ES cells are derived from a mouse strain such as CBA/Ca or C57BI/6.

95. The process of claim 94, wherein the ES cells are from the ESF116 cell line.

96. A substantially pure population of immature dendritic cells obtainable by the process of claim 64.

97. A pharmaceutical composition comprising the population of claim 96 and a pharmaceutical excipient.

98. A method of treating a patient by immunotherapy which comprise administering to a patient an effective immunotherapeutic amount of the population of claim 96.

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99. The method of claim 98, wherein the immunotherapy comprises immunostimulation.

100. The method of claim 99, wherein the immunostimulation comprises tumour immunotherapy or vaccination against infectious agents.

101. The method of claim 98, wherein the immunotherapy comprises down-modulation of a detrimental immune response.

102. The method of claim 101, wherein the down-modulation of a detrimental immune response is in the treatment of autoimmune disease or allograft rejection.

103. The method of claim 98, wherein the immunotherapy comprises altering dendritic cell function.

Sub B³ 104. The method of claim 98 or claim 103 wherein the immunotherapy comprises inducing a Th1 to Th2 immune deviation.